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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/627,447	07/24/2003	Yadong Huang	GLAD-281	3423

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EXAMINER	
LAM, ANN Y	

ART UNIT	PAPER NUMBER
1641	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/627,447	HUANG, YADONG	
	Examiner	Art Unit	
	ANN Y. LAM	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 March 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8,10-19 and 22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,10-14,19 and 20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/25/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-4, 6-8, 10-14, 19 and 20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant does not disclose that any or all carboxyl-terminal truncated apoE fragments are markers of Alzheimer's Disease. While Applicant does refer to the fragments 244-260 of apoE in claim 5, however the claims 1-4, 6-8, 10-14, 19 and 20 are not limited to that fragment.

Accordingly, the specification does not provide adequate written description of the general method as recited in claims 1-4, 6-8, 10-14, 19 and 20.

Claims 1-8, 10-14, 19 and 20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Enablement requires that the specification teach those in the art to make and use the invention without undue experimentation. Factors to be considered in determining whether a disclosure would require undue experimentation include (1) the nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the quantity of experimentation necessary, (7) the relative skill of those in the art, and (8) the breadth of the claims.

The nature of the invention:

The invention is directed toward a method for diagnosing Alzheimer's Disease in a living individual comprising detecting a level of carboxyl-terminal truncated apolipoprotein E in an aqueous biological sample.

***The state of the prior* art:**

In arguing against use of the Roses patent in the obviousness rejection, Applicant states in paragraph 10 that it has been reported in many studies that the predictive values of apoE4 genotyping do not support its utility as a diagnostic test for Alzheimer's disease. Applicant also states that a working group of the National Institute on Aging and the Alzheimer's Association recommended against the use of apoE

genotyping to predict the future development of Alzheimer's disease in asymptomatic individuals at this time, and warned against the use of the test in isolation as the sole means for diagnosing AD. Applicant gives citation in support of this declaration.

The predictability or lack thereof in the art:

The art does not disclose carboxyl-terminated apoE detected in a biological fluid (such as blood) to be predictive of the development of Alzheimer's disease or to be indicative of the presence of the disease. The art of diagnosing a disease, such as Alzheimer's disease, by detecting the presence or level of a biological molecule as a marker is highly complicated as it involves an understanding of complex biological pathways. Thus, there is a lack of predictability regarding carboxyl-terminated apoE in a biological fluid as a diagnostic indicator of Alzheimer's disease.

The amount of direction or guidance present:

Applicant does disclose in the specification on page 22 that an increase in the level of carboxyl-truncated apoE as compared to the level in a control sample from a healthy individual, of from about 25% to about 20-fold, indicates that the individual has Alzheimer's disease. Applicant also disclose on page 22 that the comparison can also be expressed as a ratio. However, given that those in the art have recommended against the use of apoE genotyping to predict the development of or to diagnose Alzheimer's disease, as mentioned in Applicant's declaration (see above), this appears to raise the question as to why carboxyl-terminated apoE (in general, or the specific fragment 244-260 of apoE) would be a reliable marker of the disease. In other words, why would detection of carboxyl-terminated apoE be a diagnostic indicator of

Alzheimer's disease when the full length apoE or its genotyping is not, as appears to be the conclusion by experts in the field? The record at present is not clear as to what evidence supports the use of carboxyl-terminated apoE to diagnose Alzheimer's disease. While Applicant states in the specification on page 22 a specific level that would indicate that an individual has Alzheimer's disease, there is no data or other evidence submitted at present to support that there is a correlation between such a level of the biomolecule and the presence of the disease and that such a level of the biomolecule can be used to diagnose the disease. Particularly in light of the conclusion by experts that the full length apoE is not considered reliable for diagnosing Alzheimer's disease, iit appears that, without evidence to show that detection of carboxyl-truncated apoE can be used to diagnose the disease, there is a lack of guidance regarding such diagnostic method. The record also lacks an explanation as to why detection of carboxyl-terminated apoE is different from detection of the full length apoE such that the warning regarding apoE by experts in the art is not applicable to carboxyl-terminated apoE as a diagnostic indicator of Alzheimer's disease. Given such lack of evidence in the record, it appears that the state of the art regarding use of the full length apoE as an unreliable marker for diagnosing Alzheimer's disease raises doubt as to whether the carboxyl-terminated apoE is enabled as a diagnostic indicator of the disease.

The presence or absence of working examples:

As noted above, Applicant states in the specification on page 22 a specific level that would indicate that an individual has Alzheimer's disease. This disclosure however

is merely an assertion of Applicant's method of detecting Alzheimer's disease, and is not a working example showing that the method actually detects Alzheimer's disease.

The quantity of experimentation necessary:

It would be undue experimentation for a skilled artisan to make and use the invention since the skilled artisan would have to provide the necessary experiments to show that the fragment is a diagnostic indicator of Alzheimer's disease.

The relative skill of those in the art:

The level of skill in the art is high.

The breadth of the claims:

Claim 5 specifically recites the detection of the fragment 244-260 of apoE. The remainder of the claims (i.e., claims 1-4, 6-8, 10-14, 19 and 20) recite carboxyl-truncated apoE in general. As discussed above, the state of the art raises doubt as to whether carboxyl-truncated apoE in general, or the fragment 244-260 of apoE, can be used as a diagnostic indicator of Alzheimer's disease.

Claims 4, 6-8, 10-14, 19 and 20 are additionally rejected on the grounds that the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, make and use the invention *commensurate in scope* with these claims, because there is absolutely no disclosure, in the specification or otherwise suggested in the art, supporting that any and all carboxyl-terminated apoE fragments can be used to diagnose Alzheimer's disease. Because claims 4, 6-8, 10-14, 19 and 20 are not limited to any *specifically disclosed* carboxyl-terminated apoE fragment, the *scope* of these claims are not enabled by the specification.

In summary, the claims are not described in the specification in such a way as to enable one to make or use the invention since there is a lack of evidence in the record that detection of carboxyl-terminated apoE or the specific fragment 244-260 of apoE can be used to diagnose Alzheimer's disease. The recommendation by experts in the art against the use of the full length apoE as a marker raises doubt as to whether the carboxyl-terminated apoE is enabled as a diagnostic indicator of Alzheimer's disease. Given the nature of the invention, state of the prior art, the lack of guidance in the art as well as by Applicant, it would require undue experimentation by one skilled in the art in order to make and use the claimed device. Claims 1-4, 6-8, 10-14, 19 and 20 are additionally rejected on the grounds that the specification does not enable one skilled in the art to make and use the invention *commensurate in scope* with these claims for the reasons set forth above.

Response to Arguments

Applicants arguments and affidavit/declaration have been considered and are found to be persuasive for the reasons set forth in the declaration. Thus, Applicant's declaration is deemed to overcome the obviousness rejection. However, the above enablement rejection was found to be appropriate.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ANN Y. LAM whose telephone number is (571)272-0822. The examiner can normally be reached on Mon.-Fri. 10-6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark Shibuya can be reached on 571-272-0806. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ann Y. Lam/
Primary Examiner, Art Unit 1641